



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS.

ACTION: Notice.

SUMMARY: Findings of research misconduct have been made against Toni M. Brand, Ph.D. (Respondent), who was a graduate student in the Department of Human Oncology, University of Wisconsin-Madison (UWM), and subsequently a research fellow in the Department of Otolaryngology - Head and Neck Surgery, University of California San Francisco (UCSF). Respondent engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Cancer Institute (NCI), National Institutes of Health (NIH), grants P30 CA014520, K99 CA160639, T32 CA108462, and U54 CA209891, National Center for Research Resources (NCRR), NIH, grant UL1 RR025011, National Center for Translational Sciences (NCATS), NIH, grants U54 TR000021 and UL1 TR000427, National Institute of General Medical Sciences (NIGMS), NIH, grant T32 GM081061, and National Institute of Dental and Craniofacial Research (NIDCR), NIH, grant R01 DE023685. The administrative actions, including supervision for a period of four (4) years, were implemented beginning on March 23, 2022, and are detailed below.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Toni M. Brand, Ph.D., University of Wisconsin-Madison and University of California San Francisco: Based on the reports of investigations conducted by UWM and UCSF and additional analysis conducted by ORI in its oversight review, ORI found that Dr. Toni M. Brand, who was a graduate student in the Department of Human Oncology, UWM, and subsequently a research fellow in the Department of Otolaryngology - Head and Neck Surgery, UCSF, engaged in research misconduct in research supported by PHS funds, specifically NCI, NIH, grants P30 CA014520, K99 CA160639, T32 CA108462, and U54 CA209891, NCRR, NIH, grant UL1 RR025011, NCATS, NIH, grants U54 TR000021 and UL1 TR000427, NIGMS, NIH, grant T32 GM081061, and NIDCR, NIH, grant R01 DE023685.

ORI found that Respondent engaged in research misconduct by knowingly or recklessly falsifying or fabricating western blot data, by reusing and relabeling data to represent expression of proteins in control experiments measuring the purity of cytoplasmic and nuclear cell fractionation, measurements of proteins of interest, and measurements of the same protein under different experimental conditions or loading controls, included in twenty-four (24) figures in the following grant application submitted to NIDCR, NIH, her Ph.D. Thesis Dissertation, and seven (7) published papers:

- K99 DE027699-01, “Targeting HPV-driven immunosuppressive signaling pathways in head and neck cancer,” submitted to NIDCR, NIH, on June 8, 2017.
- Ph.D. Thesis Dissertation, “Investigations of Nuclear HER family receptors in cancer and resistance to cetuximab therapy,” Department of Human Oncology, UWM, March 21, 2014 (hereafter referred to as “Thesis”).
- Mapping C-terminal transactivation domains of the nuclear HER family receptor tyrosine kinase HER3. *PLoS One* 2013 Aug 8;8(8):e71518; doi: 10.1371/journal.pone.0071518. eCollection 2013 (hereafter referred to as “*PLoS One* 2013”).
- Nuclear EGFR as a molecular target in cancer. *Radiother Oncol.* 2013 Sep;108(3):370-7; doi: 10.1016/j.radonc.2013.06.010 (hereafter referred to as “*Radiother Oncol.* 2013”). Corrected in: *Radiother Oncol.* 2019 Jan;130:195; doi: 10.1016/j.radonc.2018.10.011
- Nuclear epidermal growth factor receptor is a functional molecular target in triple-negative breast cancer. *Mol Cancer Ther.* 2014 May;13(5):1356-68; doi: 10.1158/1535-7163.MCT-13-1021 (hereafter referred to as “*Mol Cancer Ther.* 2014”). Corrected in: *Mol Cancer Ther.* 2019 Apr;18(4):868; doi: 10.1158/1535-7163.MCT-18-1183.
- AXL mediates resistance to cetuximab therapy. *Cancer Res.* 2014 Sep 15;74(18):5152-64; doi: 10.1158/0008-5472.CAN-14-0294 (hereafter referred to as “*Cancer Res.* 2014”).
- The receptor tyrosine kinase AXL mediates nuclear translocation of the epidermal growth factor receptor. *Sci Signal.* 2017 Jan 3;10(460):eaag1064; doi: 10.1126/scisignal.aag1064

(hereafter referred to as “*Sci Signal*. 2017”). Retracted in: *Sci Signal*. 2021 Nov

9;14(708):eabn0168; doi: 10.1126/scisignal.abn0168.

- Human Papillomavirus Regulates HER3 Expression in Head and Neck Cancer: Implications for Targeted HER3 Therapy in HPV + Patients. *Clin Cancer Res*. 2017 Jun 15;23(12):3072-3083; doi: 10.1158/1078-0432.CCR-16-2203 (hereafter referred to as “*Clin Cancer Res*. 2017”). Corrected in: *Clin Cancer Res*. 2021 Jul 15;27(14):4129; doi: 10.1158/1078-0432.CCR-21-2141.
- Cross-talk Signaling between HER3 and HPV16 E6 and E7 Mediates Resistance to PI3K Inhibitors in Head and Neck Cancer. *Cancer Res*. 2018 May 1;78(9):2383-95; doi: 10.1158/0008-5472.CAN-17-1672 (hereafter referred to as “*Cancer Res*. 2018”).

Specifically, ORI found that Respondent knowingly or recklessly falsified or fabricated data in:

- Figure 6B of Thesis and Figure 6B of *PLoS One* 2013 by reusing a Tubulin western blot panel from cytoplasmic sample to represent Histone H3 panel in nuclear sample
- Figure 6, panel C, of Thesis and Figure 6C of *PLoS One* 2013 by using identical Her3 western blot data to represent samples from different cell lines and using a Tubulin western blot panel from an unrelated experiment
- Figure 6C, inset 1, of Thesis and Figure 6C, inset 1, of *PLoS One* 2013 by inappropriately cropping the histone H3 nuclear sample to represent equal loading of the samples when the actual data showed an unequal amount

- Figure 6C, inset 2, of Thesis and Figure 6C, inset 2, of *PLoS One* 2013 by using identical Her3 western panel to represent samples from different cell lines and falsifying loading control by using a Cyclin D western blot panel to represent Tubulin
- Figure 7A and inset 2 of Thesis and Figure 7A and inset 2 of *PLoS One* 2013 by using identical Her3 western panel to represent samples from different cell lines
- Figure 2B, SKBr3 inset, of *Radiother Oncol.* 2013 by representing unrelated western panel as Tubulin loading control for the cytoplasmic samples
- Figure 2B, SUM229 inset, of *Radiother Oncol.* 2013 by representing unrelated western panel as Tubulin loading control in non-nuclear samples
- Figure 4B of *Mol Cancer Ther.* 2014 by using identical pSFKY419 western blot panels to represent expression in different cell lines
- Figure 2D of prpS6 western blot panel from HP cell line in *Cancer Res.* 2014 by using a western blot panel from an unrelated experiment
- Figure 1A of *Sci Signal.* 2017 by using identical western blot panels to represent Histone H3 in non-nuclear samples and Tubulin in nuclear samples
- Figure 2A of *Sci Signal.* 2017 by using loading control panels from an unrelated experiment in the HC8 experiment

- Figure 2C of *Sci Signal*. 2017 by using a panel from an unrelated experiment to represent histoneH3 in the nuclear samples
- Figure 2C inset of *Sci Signal*. 2017 by using a panel from an unrelated experiment to represent tubulin
- Figure 4A of *Sci Signal*. 2017 by reusing identical panels to represent tubulin (negative) control experiments
- Figure 5E of *Sci Signal*. 2017 by selective cropping and use of loading control panels from unrelated experiments
- Tubulin western blot panels in Figure 3A of K99 DE027699-01 by reusing the same data to represent two different cell lines or related data to represent a different cell line
- Figure 3A of *Clin Cancer Res*. 2017 by using the identical western blot data to represent expression of HER3 and HER3-Y1197 in the SCC47 cell line
- Supplemental Figure 3A of *Cancer Res*. 2018 by using identical western blot data to represent pAKT-S473 and pAKT-T308 expression in the SCC90 sample
- Figure 1C of *Clin Cancer Res*. 2017 and Figure 1B of K99 DE027699-01 by representing the same western blot panels to represent E6 and E7 expression in different experiments

Respondent neither admits nor denies ORI's findings of research misconduct. The parties entered into a Voluntary Settlement Agreement (Agreement) to conclude this matter without further

expenditure of time, finances, or other resources. The settlement is not an admission of liability on the part of the Respondent.

Respondent voluntarily agreed to the following:

- (1) Respondent will have her research supervised for a period of four (4) years beginning on March 23, 2022 (the “Supervision Period”). Prior to the submission of an application for PHS support for a research project on which Respondent’s participation is proposed and prior to Respondent’s participation in any capacity in PHS-supported research, Respondent will submit a plan for supervision of Respondent’s duties to ORI for approval. The supervision plan must be designed to ensure the integrity of Respondent’s research. Respondent will not participate in any PHS-supported research until such a supervision plan is approved by ORI. Respondent will comply with the agreed-upon supervision plan.
- (2) The requirements for Respondent’s supervision plan are as follows:
 - i. A committee of 2-3 senior faculty members at the institution who are familiar with Respondent’s field of research, but not including Respondent’s supervisor or collaborators, will provide oversight and guidance during the Supervision Period. The committee will review primary data from Respondent’s laboratory on a quarterly basis and submit a report to ORI at six (6) month intervals setting forth the committee meeting dates and Respondent’s compliance with appropriate research standards and confirming the integrity of Respondent’s research.

- ii. The committee will conduct an advance review of each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved. The review will include a discussion with Respondent of the primary data represented in those documents and will include a certification to ORI that the data presented in the proposed application, report, manuscript, or abstract are supported by the research record.
- (3) During the Supervision Period, Respondent will ensure that any institution employing her submits, in conjunction with each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved, a certification to ORI that the data provided by Respondent are based on actual experiments or are otherwise legitimately derived and that the data, procedures, and methodology are accurately reported in the application, report, manuscript, or abstract.
- (4) If no supervision plan is provided to ORI, Respondent will provide certification to ORI at the conclusion of the Supervision Period that her participation was not proposed on a research project for which an application for PHS support was submitted and that she has not participated in any capacity in PHS-supported research.
- (5) During the Supervision Period, Respondent will exclude herself voluntarily from serving in any advisory or consultant capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee.
- (6) Respondent will request that the following papers be corrected or retracted:

- *PLoS One* 2013 Aug 8;8(8):e71518

- *Cancer Res.* 2014 Sep 15;74(18):5152-64
- *Cancer Res.* 2018 May 1;78(9):2383-95

Respondent will copy ORI and the Research Integrity Officers at UWM and UCSF on the correspondence with the journals.

Dated: April 5, 2022.

Wanda K. Jones,

Acting Director, Office of Research Integrity,

Office of the Assistant Secretary for Health.

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